

PET-BIDS, an extension to the brain imaging data structure for positron emission tomography

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ABSTRACT

The Brain Imaging Data Structure (BIDS) is a standard for organizing and describing neuroimaging datasets. It serves not only to facilitate the process of data sharing and aggregation, but also to simplify the application and development of new methods and software for working with neuroimaging data. Here, we present an extension of BIDS to include positron emission tomography (PET) data (PET-BIDS). We describe the PET-BIDS standard in detail and share several open-access datasets curated following PET-BIDS. Additionally, we highlight several tools which are already available for converting, validating and analyzing PET-BIDS datasets.

44 Background & Summary

45 Positron Emission Tomography (PET) was developed in the late 1950s with the ultimate goal of measuring and visualizing
46 physiological processes *in vivo* such as metabolism, blood flow and the concentration of proteins in various receptor systems¹⁻³.
47 Since then, PET has been used extensively in pre-clinical and clinical settings, mostly for oncological purposes⁴, but
48 increasingly also in areas of cardiology and neurology (for investigation of, e.g., synaptic plasticity, neuroinflammation, and
49 neurodegeneration⁵). For brain imaging specifically, PET has largely been applied together with high affinity radiolabeled
50 molecules to quantify the brain's distribution, concentration and drug occupancy of proteins, using pharmacokinetic models⁶.
51 The outcomes of this work have provided significant insights into the complex neurobiology of receptor systems in the healthy
52 and diseased brain, as well as advancements in our understanding of pharmacological treatments⁶. However, compared to
53 imaging modalities such as structural Magnetic Resonance Imaging (MRI), experiments using PET often involve data from
54 multiple sources including, e.g., chemical characteristics of radiolabelled molecules and blood and metabolite data acquired
55 during the imaging procedure (Figure 1). The acquisition and availability of different types of data related to the PET experiment
56 depends on the biological target of interest, and complicates the standardization of the acquired data for storage, analysis and
57 sharing. Furthermore, due to differences in PET scanner vendors and blood sampling devices across PET centers, data are often
58 stored in different file formats, and with varying nomenclature describing the same type of data. Historically, the field of PET
59 brain imaging attained maturity with the adoption of a consensus nomenclature for pharmacokinetic modeling of PET data in
60 2007⁷. Recently in 2020, similar to the Organization for Human Brain Mapping recommendations from the Committee on Best
61 Practices in Data Analysis and Sharing (COBIDAS) for MRI and MEEG, consensus guidelines for describing the content and
62 format of PET brain data in publications and archives has emerged⁸.

63 The Brain Imaging Data Structure (BIDS) standard was originally developed for MRI as a community standard for organizing
64 and sharing brain imaging study data within and between laboratories⁹. While the focus was originally targeting MRI, and
65 especially structural and functional MRI (fMRI), BIDS has since rapidly expanded to include many different imaging modalities,
66 including magnetoencephalography (MEG)¹⁰, electroencephalography (EEG)¹¹, intracranial electroencephalography (iEEG)¹²,
67 and linking brain imaging to genetics¹³. BIDS mainly addresses the heterogeneity of data organization by following the
68 FAIR principles (findability, accessibility, interoperability, and reusability)¹⁴. Findability and reusability are addressed in
69 BIDS by providing rich metadata in dedicated sidecar files. Interoperability is addressed by using the existing Neuroimaging
70 Informatics Technology Initiative (NIFTI) format for storing brain imaging data, text files arranged according to the JavaScript
71 Object Notation (JSON) format for complementary metadata, and Tab Separated Value (TSV) format for tabular data. While
72 accessibility is not directly addressed within the BIDS standard itself, the existence of such a standard facilitates the development
73 of public data repositories. The largest of these repositories, OpenNeuro (<https://openneuro.org>), is already built
74 around the BIDS standard, and a new repository fully dedicated to PET scans (OpenNeuroPET) is currently under development
75 (<https://openneuro.org/pet>). BIDS also fosters interoperability and reuse of already acquired data by defining how
76 to structure and store data using naming conventions and dedicated metadata files. Because BIDS data follow a common
77 data structure and description, the proliferation of BIDS datasets incentivizes the creation of analysis pipelines that target this
78 structure, the adoption of which promotes verifiable and reproducible research practices.

79 In this work, we present the main features of the extension of BIDS to include PET data (PET-BIDS). This extension largely
80 builds upon the original BIDS specification⁹, and the guidelines for the content and format of brain PET data in publications
81 and archives⁸. The full documentation of the PET-BIDS extension can be found in the general BIDS specification¹.

82 PET-BIDS summary

83 The extension of BIDS to include PET data largely aligns with the BIDS specification for other imaging modalities, describing
84 a way for organizing PET data and specifying metadata for PET experiments. A rough overview of the directory structure is
85 given in Figure 2, and a detailed example is given in Figure 3. Each subject's data corresponds to a directory which contains
86 subdirectories for each acquisition session (e.g., *baseline*, *rescan* or *intervention*) and imaging modality (e.g., *pet*). The
87 subdirectories are also accompanied by a `dataset_description.json` file containing generic information about the
88 dataset, providing full credit to the authors sharing the data. Within each subject directory, the `/pet` subdirectory contains the
89 PET imaging data and the corresponding metadata. PET imaging data are stored in 4D (or 3D if only one volume was acquired)
90 NIFTI files with a `_pet` suffix. When acquiring several volumes (frames in PET terminology) these should be stored in 4D in
91 chronological order (the order they were acquired in). The imaging data are accompanied by a `_pet.json` sidecar file which
92 details the metadata of the PET acquisition. All the metadata are in accordance with the guidelines for the content and format
93 of brain PET data⁸.

94 The file naming structure for PET data closely follows the general BIDS guidelines⁹, using specified key-value pairs
95 joined by hyphens and separated by underscores. Multiple sessions (typically visits) are encoded by adding an extra layer

¹<https://bids-specification.readthedocs.io/en/stable/>

96 of directories in the form of `ses-<label>`. Hence, a single session study, `sub-<label>` would have a subdirectory
97 `/pet` which contains PET files using the naming pattern `sub-<label>_ses-<label>_pet.nii[.gz]` corresponding
98 to several acquisitions of PET data. The session label should be used in cases such as test-retest or baseline-intervention
99 setups. Additionally, a `task-<label>` can be inserted in a similar way as task-based and resting state Blood Oxygen Level
100 Dependent (BOLD) fMRI data in the existing BIDS standard. For example, in the case of studies using combined PET/fMRI,
101 subject-specific tasks may be carried out during the acquisition within the same session. Therefore, it is possible to specify
102 `task-<label>` in accordance with the fMRI data. Specifically for PET, multiple acquisitions per subject using different
103 tracers during the same session are possible and the `trc-<label>` must be used to distinguish between different tracers.
104 Please keep in mind that the label used is arbitrary and each file requires a separate JSON sidecar file with details of the
105 tracer used. Also, specifically for PET a reconstruction key `rec-<label>` can be used to distinguish different types of
106 reconstructions of the PET data. The `rec-<label>` has four reserved values: *acdyn*, for reconstructions with attenuation
107 correction of dynamic data; *acstat*, for reconstructions with attenuation correction of static data; *nacdyn*, for reconstructions
108 without attenuation correction of dynamic data; *nacstat*, for reconstructions without attenuation correction of static data.
109 Further information about the reconstruction should be added to the accompanying `_pet.json` metadata file. Finally, the
110 `run-<index>` can be used if one scan type/contrast is repeated multiple times within the same scan session/visit. For
111 example, for dynamic PET acquisitions, subjects may have to leave the scanner to use the bathroom. While leaving the scanner
112 would interrupt an MR acquisition, in PET this disruption is more appropriately considered missing data during a run, and the
113 acquisition would still be considered the same session/run. However, there are also cases of acquisitions where this definition
114 might not be entirely clear, and it will be up to the researcher to decide what makes most sense. For example, dual-time-window
115 acquisitions¹⁵ could be considered two runs within the same session, but it could also be considered a single run with missing
116 data between the two time windows.

117 **Blood data availability**

118 If blood data are available, such as arterial or venous samples acquired during the PET experiment, they are stored in the
119 `/pet` folder alongside the corresponding PET data (Figure 3). Blood can be sampled by an autosampler, for continuous
120 monitoring of whole blood radioactivity, and/or manually drawn for discrete blood samples. Therefore, the recording key
121 `recording-<label>` for blood data has two reserved values: 1) *autosampler*, and 2) *manual*. The blood metadata should
122 be stored in a JSON sidecar file with a `recording-<label>` and a `_blood` suffix, containing information about what
123 blood data are available (e.g. radioactivity in plasma and/or whole blood and parent compound). The blood JSON sidecar file
124 should be accompanied by a tabular TSV file with similar naming convention, containing all the values of the available blood
125 data. All blood data should be reported according to a unique reference time-scale in relation to a predefined time zero defined
126 by the PET data (Figure 1). The definition of time zero will be further explained below.

127 **Specific PET-BIDS considerations**

128 In order to construct the `_pet.json` sidecar file which details the PET experiment metadata, a description of a common PET
129 experiment is necessary. In Figure 1 we present an overview of a common PET experiment (which includes the sampling of
130 blood data, including plasma, whole blood and metabolite data). The experiment is defined on a single time scale relative to a
131 predefined “time zero”. Notably, “time zero” will often be defined as time of injection or scan start, and the injected dose, the
132 PET data, and blood data should optimally all be decay-corrected to time zero. However, because the time of injection does not
133 always coincide with scan start, PET data may not be decay-corrected to the time of injection. Whether the image has been
134 decay-corrected may be indicated in its metadata (using the fields: *ImageDecayCorrected* and *ImageDecayCorrectionTime*).
135 The flexibility in choice of time zero to either scan start or injection time was chosen to maximize ease of use and adoption
136 of PET-BIDS by the broadest possible spectrum of the PET community, due to potentially large differences in experimental
137 design between PET studies. For example, scan start and injection time may not always coincide, and due to radioactive decay
138 of the radiotracer, it is important to be aware of post-hoc decay correction. Importantly, the injected dose should always be
139 decay corrected to the time of injection.

140 Across the diverse set of radiotracers and experimental designs in PET, it will not always be possible to enter the required
141 metadata following the guidelines for sharing of PET data⁸. For example, while the injected mass and specific radioactivity are
142 required metadata according to the guidelines⁸, this is not possible to measure for certain radiotracers such as [¹⁸F]FDG due
143 to its mass being too low to measure. In these cases, the values for injected mass and specific activity may be set to “n/a” to
144 indicate missing values. We note that for required metadata, this is currently only valid for injected mass and specific activity,
145 although future releases of the PET-BIDS specification may tackle further challenges in use cases that deviate from the current
146 guidelines.

147 In the case of including MRI data with PET data, it is necessary to pay specific attention to the format the MR images are in,
148 such as whether they have been unwrapped to correct for gradient non-linearities. There is a specific metadata field in the BIDS

149 specification for MRI⁹ named *NonlinearGradientCorrection* which indicates this (please see Figure 3 for an example). The
150 main reason for the importance of this is that the MRI needs to be corrected for nonlinear gradients causing spatial distortions
151 in order to have the same shape as the accompanying PET scans for co-registration⁸. Therefore, it is required to specify
152 whether the corresponding MR images have been corrected for gradient non-linearities, using the *NonLinearGradientCorrection*
153 metadata field, if PET data are present.

154 In general, SI units must be used to describe the data such as "Bq/mL" for radioligand concentration, and seconds for time
155 measurements relative to either scan start or injection time ("time zero").

156 Public PET-BIDS datasets

157 Several example datasets (with zero-byte, i.e., empty, NIfTI files) are publicly available in the BIDS-examples GitHub repository
158 (<https://github.com/bids-standard/bids-examples>). The first two of these datasets (full version) are also
159 openly available on OpenNeuro formatted using the PET-BIDS standard:

- 160 • The CIMBI Database [¹¹C]DASB PET Example Dataset consists of test and retest measurements from two individuals to
161 measure serotonin transporter availability¹⁶. No blood data are available for this dataset. It was collected as a part of the
162 CIMBI database (<https://doi.org/10.18112/openneuro.ds001420.v1.0.1>)¹⁷.
- 163 • The NRM2018 Grand Challenge dataset consists of baseline and intervention data from five individuals. No blood data
164 are available for this dataset (<https://doi.org/10.18112/openneuro.ds001705.v1.0.1>)¹⁸.
- 165 • The CIMBI Database [¹¹C]CIMBI-36 PET Example Dataset consists of a single dynamic PET measurement of a pig to
166 measure serotonin 2A receptor availability. Blood and metabolite data are available for this dataset. It was collected as
167 a part of the CIMBI database ([https://github.com/bids-standard/bids-examples/tree/master/
168 pet001](https://github.com/bids-standard/bids-examples/tree/master/pet001)).
- 169 • The CIMBI Database [¹¹C]CIMBI-36 Intervention Example Dataset consists of a single dynamic PET measurement of a
170 pig using bolus-infusion, and with a pharmacological ketanserin intervention during the scan. Blood and metabolite data
171 are available for this dataset ([https://github.com/bids-standard/bids-examples/tree/master/
172 pet004](https://github.com/bids-standard/bids-examples/tree/master/pet004)).
- 173 • The CIMBI Database [¹¹C]AZ10419369 Visual Stimuli Example Dataset consists of two dynamic PET measurements
174 of a single subject using combined PET/MRI. The first scan is a baseline scan, whereas the second scan includes a
175 visual stimuli task during the scan. No blood data are available for this dataset. It was included in Hansen et al. 2020¹⁹
176 (<https://github.com/bids-standard/bids-examples/tree/master/pet005>).

177 Community tools for data sharing and analysis

178 The BIDS validator

179 Data curated into the PET-BIDS standard can be validated for BIDS compliance by using the "bids-validator"²⁰, a JavaScript
180 application checking for the completeness and consistency of the data. The BIDS validator runs locally as a command line
181 version (via Node.js), as a Docker container, or as a browser-based application ([https://bids-standard.github.
182 io/bids-validator/](https://bids-standard.github.io/bids-validator/)). Using this important validation software, PET researchers are provided with feedback about
183 incompatibility errors as well as warnings if important pieces of metadata are missing. In addition to providing a version of
184 the validator as open source software, we are collaborating with the software developers of major PET analysis tools (PMOD,
185 SPM, MIAKAT and PETsurfer²¹) to facilitate rapid adoption and support of this format, and working with major PET centres
186 to help PET researchers convert their data into PET-BIDS format. Several software tools already exist to convert dicom files
187 and ECAT data into BIDS format, such as dcm2niix²² (<https://github.com/rordenlab/dcm2niix>), however, the
188 output may need *post-hoc* editing if required metadata are not available in the imaging header files.

189 The BIDS starter kit

190 The BIDS starter kit is a tool to help researchers get started with the BIDS data structure ([https://github.com/
191 bids-standard/bids-starter-kit](https://github.com/bids-standard/bids-starter-kit)). It consists of a collection of community-driven guides, tutorials, helper
192 scripts, and wiki resources. A tutorial that describes how to create a BIDS-compatible PET data set has been provided on
193 the starter-kit wiki (<https://github.com/bids-standard/bids-starter-kit/wiki>), and MATLAB (bids-
194 matlab; <https://github.com/bids-standard/bids-matlab>) and Python (pybids; [https://github.com/
195 bids-standard/pybids](https://github.com/bids-standard/pybids)) packages are also available to produce and/or work with PET sidecar JSON and TSV files.
196 These packages are freely available on GitHub.

197 Sharing of acquired PET data

198 According to the guidelines for the content and format of brain PET data⁸, acquired PET data are defined as PET data after
199 reconstruction into 3D or 4D frames. These data may be shared in repositories such as OpenNeuro (<https://openneuro.org>),
200 which is an open archive for analysis and sharing of public neuroimaging data spearheading the movement of best
201 practices within MRI, MEG, EEG, iEEG, ECoG, ASL and now PET²³. The OpenNeuro platform is the successor of OpenfMRI
202 (established in 2011, <https://openfmri.org/>), and the project enjoys relatively wide acceptance by the field and
203 capitalizes on the BIDS standard. It has been running for almost a decade and is one of the fastest growing image databases,
204 with about 12 new datasets being added per month. All datasets on OpenNeuro are validated for BIDS compliance prior to
205 upload.

206 Data analysis pipelines and sharing of derived PET data

207 BIDS also offers the possibility to build fully reproducible analysis workflows using the concept of BIDS applications²⁴. A
208 BIDS application is a software container capturing all the dependencies of a neuroimaging analysis pipeline (e.g., fMRIPrep)
209 that takes a BIDS formatted data set as input. Each BIDS application has the same core set of command line arguments, making
210 them easy to run and integrate into automated platforms, allowing for full computational reproducibility. Several open-source
211 initiatives for PET are currently under development to BIDS applications, including PETSURFER (<https://surfer.nmr.mgh.harvard.edu/fswiki/PetSurfer>), APPIAN (<https://github.com/APPIAN-PET/APPIAN>) and
212 kinfitr (<https://github.com/matheson/kinfitr>) providing tools to carry out preprocessing and/or pharma-
213 cokinetic modeling of PET data. We also highly recommend the great resources by the TURKU PET centre (<http://www.turkupetcentre.net/>),
214 which have been providing thorough documentation and analysis tools for PET for
215 several decades. The resulting outputs from BIDS applications can be shared using BIDS derivatives standards, describing
216 the outputs of common preprocessing pipelines and pharmacokinetic models. The specification for PET-BIDS derivatives
217 (BIDS Extension Proposal 23) is currently under development, and will capture data and metadata sufficient for a researcher to
218 understand and reuse the output of a common PET analysis pipeline, including preprocessing and pharmacokinetic modeling.
219

220 Conclusion

221 The PET extension to BIDS specifies a structured way of storing PET data and metadata. BIDS is a community-driven project,
222 and the PET-BIDS specification was created in a joint effort made by the PET community (open and with community peer
223 review) aligning with the consensus guidelines for the content and format of PET brain data in publications and archives⁸.
224 PET-BIDS will make data sharing and software development easier, facilitate rapid development, adoption and application of
225 new tools and methods, and ultimately foster collaboration between researchers to combine data sets from different centers to
226 achieve larger sample sizes and improved statistical power to test hypotheses.

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283 Author contributions statement

284 MG and MN: Conception and design of the specification, moderating community interactions, coding of the bids-validator

285 extension, preparation of datasets and examples, writing the manuscript. GJM: critical review and editing of the specification,

286 coding of PET-BIDS tools (KinFitr), final review of the version submitted. HDH, AT, GS, GR, MV, AG, MY, MT, TF, AG, HB,

287 AR, JRD, TB, FF, CJM, KJG, RWB, SA, RG, TS, GN, CP, CP, RO, JG, REC, GMK, RBI: critically reviewed the specification

288 and final approval of the version submitted.

289 Competing interests

290 The authors declare no competing interests.

291 Figures & Tables

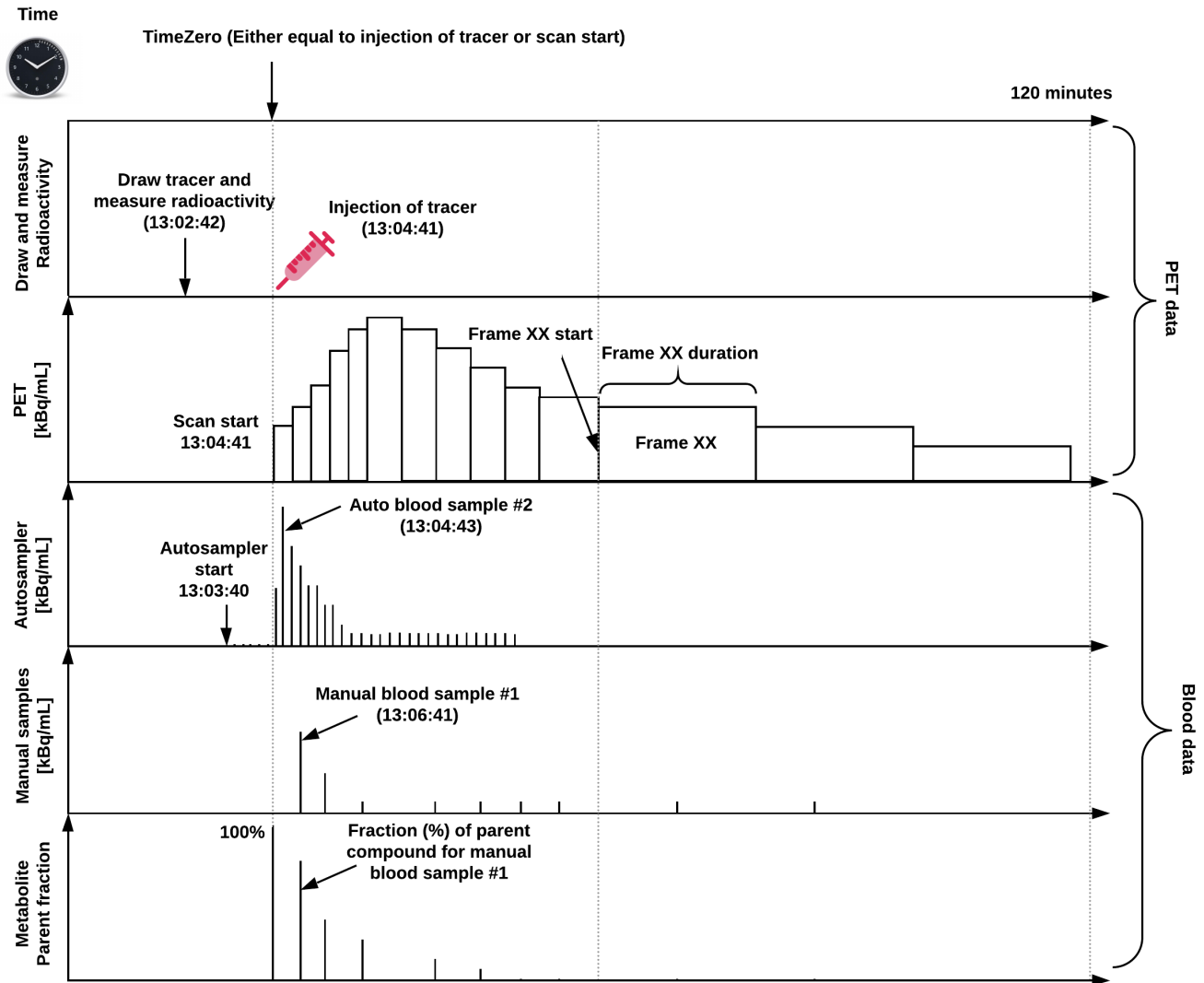


Figure 1. Overview of a common PET experiment, including blood measurements, and defined on a common time scale. Note, “time zero” can either be defined as time of injection or scan start, and all the PET and blood data should be decay-corrected to this time point.

```

sub-<participant_label>/
  ses-<session_label>/
    pet/
      sub-<participant_label>[_ses-<session_label>][_task-<task_label>]...
      ...[_trc-<label>][_rec-<label>][_run-<index>]_pet.nii.gz
      sub-<participant_label>[_ses-<session_label>][_task-<task_label>]...
      ...[_trc-<label>][_rec-<label>][_run-<index>]_pet.json
  
```

Figure 2. The template for the naming convention of the PET-BIDS file structure. The naming convention follows a key-value pair defining various steps of the acquisition, including the session, task, acquisition, reconstruction, and run. The main imaging data file has a `_pet` suffix stored in the NIfTI format (*.nii). The imaging data are accompanied by a JSON sidecar file containing all the necessary metadata needed to understand the PET data.

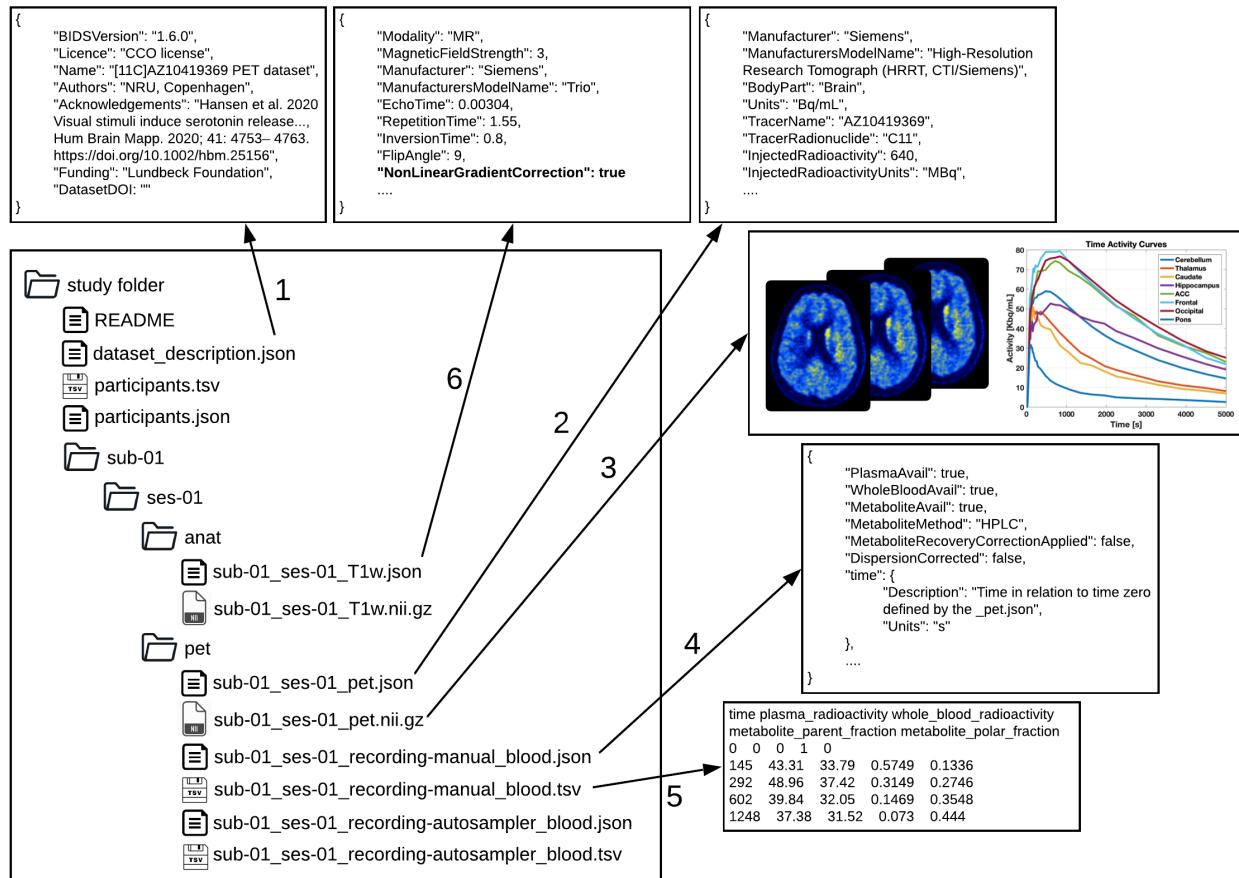


Figure 3. Exemplary PET-BIDS dataset with a dataset description, including adequate acknowledgements (1), previews of PET files (2,3), including blood (4,5) and MRI data (6). The left side shows a directory tree of a common PET-BIDS dataset, with files in the root directory describing the dataset (README and data_description.json), a file with participant-specific information (participants.tsv), and a JSON sidecar file describing the metadata needed to understand the corresponding TSV file. Next to the files in the root directory, there are subject directories named sub-<label> for each study participant. In the subject directory lies all acquired data divided into modalities (anat and pet, for the PET and structural MRI, respectively). The content of the pet directory are displayed in the right side of the figure, including the metadata of the raw PET data (2), and the associated imaging data (3). The metadata for the blood data acquired using manual sampling is stored in a JSON sidecar file (4), with the corresponding blood specified in the TSV file (5). The columns in the TSV file contain 1) time, 2) plasma radioactivity, 3) whole blood radioactivity, 4) metabolite parent fraction, and 5) metabolite polar fraction. Blood data acquired using an autosampler is also available following a similar structure as (3) and (4). The PET data may be accompanied with MRI data for co-registration and region definition (6). In this case, it is required to specify if the MRI data has been corrected for gradient non-linearities (*NonLinearGradientCorrection*) to allow for correct co-registration with the PET data.